

SUPPORTING INFORMATION

Figure S1. Linkage disequilibrium (LD) structure across 32 kbp of genomic region encompassing the rs688 locus as estimated among all genotyped SNPs on the CEU sample available from HapMap. A standard color scheme is used to display LD with bright red color for very strong LD ($LOD = 2$ $D' = 1$), white color for no LD ($LOD < 2$, $D' < 1$), pink red ($LOD = 2$ $D' < 1$), and blue ($LOD < 2$ $D' = 1$) for intermediate LD. Values in boxes represent the pair-wise r^2 measure between markers.

Figure S2. LDLR exon 12 splicing efficiency in LCLs. (A) *LDLR* exon 12 splicing efficiency was calculated as *LDLR 12(+)*/total *LDLR*. (B) *LDLR* total mRNA copy number was log transformed. For C/C, T/C, and T/T, n=46, 90, 37, respectively (A) and n=382, 311, 109, respectively. *LDLR* total mRNA was quantified by expression array as previously described (S1). All data were adjusted for age, sex, race, smoking and BMI. P-values were calculated with two tailed t-tests. Values plotted are mean \pm s.e.m.

REFERENCE:

S1 Medina MW, *et al.* (2012) RHOA is a modulator of the cholesterol lowering effects of statin *PLoS Genetics* in press

Figure S3. Scatter plot analysis of fluorophore colocalization. Scatter plots (A: rs688 “C” and B: “T”) were plotted for the intensity of green (LDLR) plotted against the intensity of red (lysosome) for each pixel and the Coefficients of Determination were determined by Zeiss Zen software.

Figure S4. Effect of rs2228671 on PCSK9 regulation of LDLR. (A) HepG2 cells were transiently transfected with a plasmid expressing LDLR containing either rs2228671 “T” or “C”, and incubated with DiI-LDL (10µg/ml) mixed with purified PCSK9 protein (0, 2µg/ml, 20µg/ml) for 5 hours. DiI-LDL uptake was determined (n=8). (B) Exogenous PCSK9 protein (2µg/ml) was preincubated with varying concentrations of IB20, a PCSK9-antibody, and subsequently mixed with DiI-LDL (10µg/ml). Rate of DiI uptake was quantified in transiently transfected HepG2 cells (n=8) as described in part A. *MFI: Mean Fluorescence Intensity.

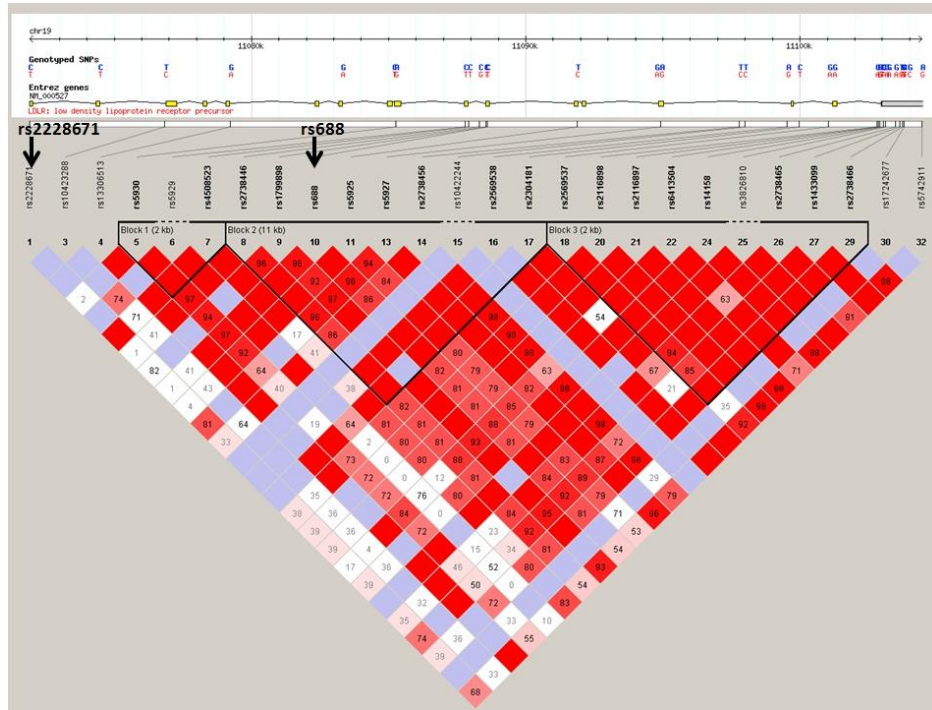


Figure S1

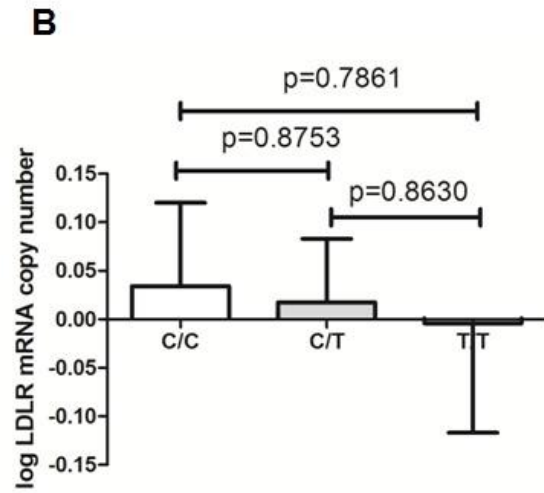
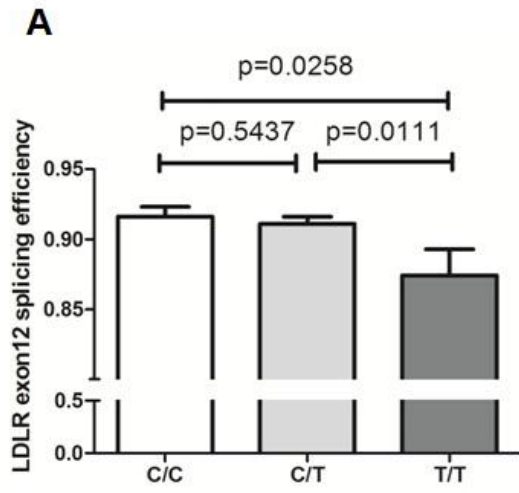


Figure S2

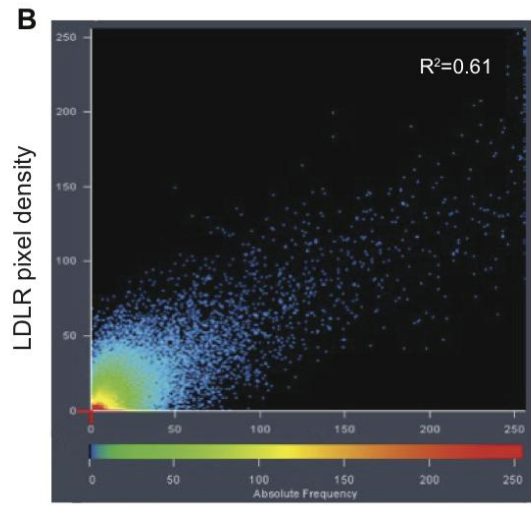
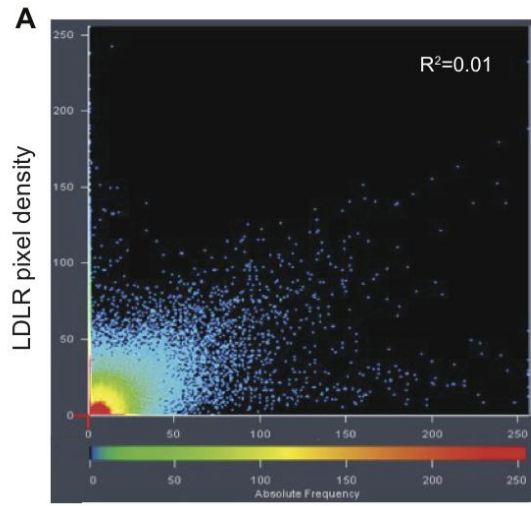


Figure S3

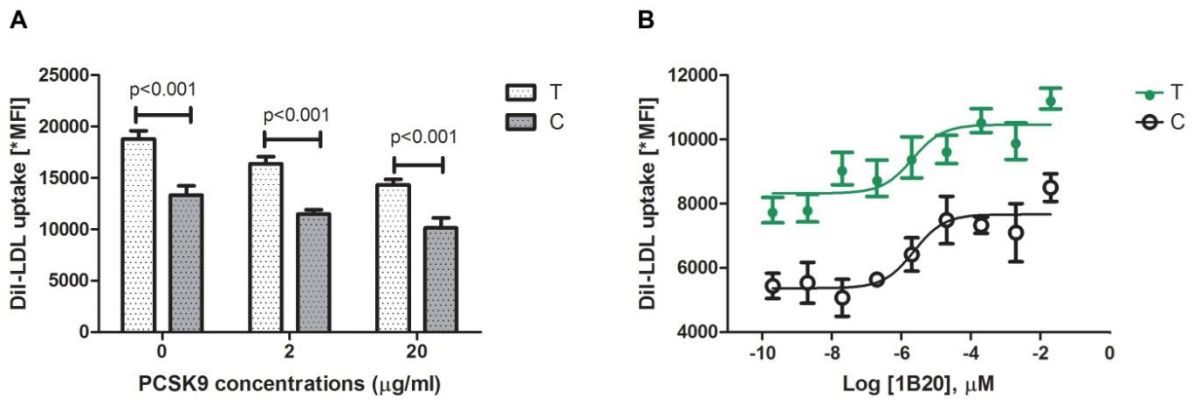


Figure S4